b.) Amendments to the Claims:

Applicants presently amend claims 12, 37, 39-40, 52, 55, 57-58 and add new claims 233 and 234. All other pending claims are canceled. As of this amendment and response, claims 12, 37, 39-40, 52, 55, 57-58, and 233-234 are pending. The status modifiers below indicate that status of the claims as of this response. The examiner notes that, as of the office action of February 23, 2004, claims 1-227 are pending. Applicants believe that claims 1-232 were pending as of that office action. Applicants respectfully direct the examiner's attention to their remarks on page 3 of their response to the office action of June 18, 2003. Applicants had submitted a Preliminary Amendment in the present application on June 23, 2000. In a telephone discussion with Examiner Borin on May 6, 2003, Applicants learned that this amendment was never entered. As per instructions from Examiner Borin, in their response of June 18, 2003 the applicants appended a copy of the Preliminary Amendment along with a copy of the return postcard evidencing the submission of the amendment. As agreed to by the examiner, Applicants then proceeded as if the Preliminary Amendment were entered, and subsequent changes made were made with respect to the claims entered in that amendment. Accordingly, claims 1-232 are pending as of the office action of February 23, 2004. Additionally, claims 15-27 are canceled as of this response, which should clarify any uncertainty regarding their status.

1-11. (Canceled)

12. (Currently Amended) ~~An~~ A DAOCS or DOACS/DACS enzyme comprising a modification at the site which binds the side chain of penicillin N, and wherein at least one ~~enzyme having significant sequence similarity to DAOCS, wherein the side chain binding site of DAOC is modified and~~ amino acid residue at one or more of the following sites of said enzyme selected from the group consisting of Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, and Asn304; is changed to another amino acid residue or is deleted.

13 - 36. (Canceled).

37. (Previously Added) The enzyme of claim 12, further comprising the insertion or deletion of at least one additional amino acid residue within the region 300-311.

38. (Canceled).

39. (Currently Amended) ~~An~~ A DAOCS or DOACS/DACS enzyme comprising a modification at the site which binds the side chain of penicillin N, and wherein at least one ~~enzyme having significant sequence similarity to DAOCS, wherein the side chain binding site of DAOC is modified and~~ amino acid residue at one or more of the following sites of said enzyme selected from the group consisting of ~~Thr72, Arg74, Arg75, Glu156, Leu158, Arg160, Arg162, Leu186, Ser187, Phe225, Phe264, Arg266, Asp301, Tyr302, Val303, and Asn304~~ Ile88, Leu158, Arg160, Arg162, Phe164, Met180, Thr190, Ile192, Phe225, Pro241, Val245, Val262, Phe264, Ile305, Arg306 and Arg307; is changed to another amino acid residue or is deleted.

40. (Currently Amended) The enzyme of claim 12, further comprising the insertion or deletion of at least one additional amino acid residue within the region 300-311.

41 - 51. (Canceled).

52. (Currently Amended) An enzyme as claimed in claim ~~14~~ 12, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

53 – 54 (Canceled).

55. (Previously Presented) An enzyme as claimed in claim 37, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

56. (Canceled).

57. (Previously Presented) An enzyme as claimed in claim 39, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

58. (Previously Presented) An enzyme as claimed in claim 40, wherein two or more complementary mutations are introduced to create or delete a binding interaction, including H-bonds, electrostatic, or hydrophobic interactions.

59 – 232 (Canceled).

233. (New) An enzyme according to claim 12 which is a *Streptomyces clavuligerus* enzyme.

234. (New) An enzyme according to claim 39 which is a *Streptomyces clavuligerus* enzyme.